

WHAT IS CLAIMED IS:

1. A method of killing a cell, comprising contacting a cell
with a p53 protein or gene and a DNA damaging agent in a combined
amount effective to kill said cell.

2. The method of claim 1, wherein said cell is contacted with a
p53 protein or gene in combination with X-ray radiation,
UV-irradiation, γ -irradiation, microwaves, adriamycin,
5-fluorouracil, etoposide, camptothecin, actinomycin-D,
mitomycin C, or cisplatin.

3. The method of claim 2, wherein said cell is contacted with a
p53 protein or gene in combination with cisplatin.

4. The method of claim 1, wherein said cell is contacted with a
recombinant vector that expresses a p53 protein in said cell in
combination with a DNA damaging agent.

5. The method of claim 4, wherein said p53-expressing
recombinant vector is a naked DNA plasmid, a plasmid within a
liposome, a retroviral vector, an AAV vector, or a recombinant
adenoviral vector.

6. The method of claim 5, wherein said p53-expressing
recombinant vector is a recombinant adenoviral vector.

Sub 43
7. The method of claim 6, wherein said p53-expressing recombinant vector is a recombinant adenoviral vector comprising a p53 expression region positioned under the control of the cytomegalovirus IE promoter.

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8. The method of claim 6, wherein said recombinant adenoviral vector comprises a p53 expression region, the cytomegalovirus IE promoter and the SV40 early polyadenylation signal.

Sub F2
9. The method of claim 6, wherein at least one gene essential for adenovirus replication is deleted from said adenovirus vector construct and the p53 expression region is introduced in its place.

10. The method of claim 9, wherein the E1A and E1B regions of the adenovirus vector are deleted and the p53 expression region is introduced in their place.

11. The method of claim 6, wherein said recombinant adenoviral vector is present within a recombinant adenovirus.

12. The method of claim 1, wherein said cell is first contacted with a p53 protein or gene and is subsequently contacted with a DNA damaging agent.

Sub C3
13. The method of claim 1, wherein said cell is first contacted with a DNA damaging agent and is subsequently contacted with a p53 protein or gene.

14. The method of claim 1, wherein said cell is simultaneously contacted with a p53 protein or gene and a DNA damaging agent.

15. The method of claim 2, wherein said cell is contacted with a first composition comprising a p53 protein or gene and a second composition comprising a DNA damaging agent.

10 16. ¹⁵ The method of claim ¹⁴ 15, wherein said first or second composition is dispersed in a pharmacologically acceptable formulation.

15 17. The method of claim 1, wherein said cell is contacted with a single composition comprising a p53 protein or gene in combination with a DNA damaging agent.

20 18. ¹⁷ The method of claim ¹⁶ 17, wherein said composition is dispersed in a pharmacologically acceptable formulation.

25 19. The method of claim 17, wherein said cell is contacted with a single composition comprising a recombinant vector that expresses p53 in said cell in combination with a DNA damaging agent.

20. The method of claim 19, wherein said cell is contacted with a single composition comprising a recombinant adenovirus containing a recombinant vector that expresses p53 in said cell in combination with a DNA damaging agent.

Sub 3
21. The method of claim 1, wherein said cell is a human cell.

22. The method of claim 1, wherein said cell is a malignant cell.

23. The method of claim 22, wherein said cell is a lung cancer cell.

24. The method of claim 22, wherein said cell is a breast cancer cell.

25. The method of claim 22, wherein said cell has a mutation in a p53 gene.

26. The method of claim 1, wherein said cell is located within an animal and said p53 protein or gene and DNA damaging agent are administered to the animal in a pharmacologically acceptable form.

27. A method of treating cancer, comprising administering to an animal with cancer a therapeutically effective combination of a p53 protein or gene and a DNA damaging agent.

28. The method of claim 27, comprising injecting into a tumor site a therapeutically effective amount of a pharmaceutical composition comprising a recombinant adenovirus containing a

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recombinant vector that expresses p53 in the tumor cell, and
contacting the tumor with a DNA damaging agent.

5 29. The method of claim 28, wherein the tumor is contacted with
a DNA damaging agent by irradiating the tumor site with X-ray
radiation, UV-irradiation, γ -irradiation or microwaves.

10 30. The method of claim 28, wherein the tumor is contacted with
a DNA damaging agent by administering to the animal a
therapeutically effective amount of a pharmaceutical composition
comprising a DNA damaging compound.

15 31. The method of claim 28, wherein the DNA damaging compound is
cisplatin.

20 32. A composition comprising a p53 protein or gene in
combination with a DNA damaging agent.

25 33. The composition of claim 32, comprising a p53 protein or
gene in combination with adriamycin, 5-fluorouracil, etoposide,
camptothecin, actinomycin-D, mitomycin C, or cisplatin.

*See
C7*
30 34. The composition of claim 33, comprising a p53 protein or
gene in combination with cisplatin.

Sub 37
cont
35. The composition of claim 32, comprising a recombinant vector that expresses a p53 protein in an animal cell in combination with a DNA damaging agent.

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Sub 37
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36. The composition of claim 35, wherein said recombinant vector is a naked DNA plasmid, a plasmid within a liposome, a retroviral vector, an AAV vector, or a recombinant adenoviral vector.

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37. The composition of claim 36, wherein said recombinant vector is a recombinant adenoviral vector.

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38. The composition of claim 37, wherein said recombinant vector is a recombinant adenoviral vector is present within a recombinant adenovirus particle.

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39. The composition of claim 32, comprising a recombinant adenoviral vector present within a recombinant adenovirus particle in combination with cisplatin.

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40. The composition of claim 32, dispersed in a pharmacologically acceptable formulation.

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41. The composition of claim 40, formulated for intralesional administration.

Sub 38
42. A therapeutic kit comprising, in suitable container means, a pharmaceutical formulation of a recombinant vector that expresses

Sub C.8
a p53 protein in an animal cell and a pharmaceutical formulation of a DNA damaging agent.

5 ³⁵ 43. The kit of claim ~~42~~³⁴, wherein said recombinant vector and said DNA damaging agent are present within a single container means.

10 ³⁶ 44. The kit of claim ~~42~~³⁴, wherein said recombinant vector and said DNA damaging agent are present within distinct container means.

15 ³⁶ 45. The kit of claim ~~42~~³⁴, comprising a pharmaceutical formulation of a recombinant adenovirus including a recombinant vector that expresses a p53 protein in an animal cell and a pharmaceutical formulation of cisplatin.

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